

Dean L. Engelhardt, et al.

Serial No.: 08/479,997

Filed: June 7, 1995

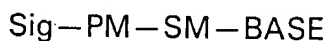
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KINDLY AMEND THE ABOVE-IDENTIFIED APPLICATION AS FOLLOWS:

In The Claims:

Please enter new claims 576-825 as follows:

1 ~~576.~~ An oligo- or polydeoxyribonucleotide which is complementary to a nucleic acid of interest or a portion thereof, said oligo- or polydeoxyribonucleotide comprising at least one modified nucleotide having the formula



N¹ wherein PM is a phosphate moiety, SM is a sugar moiety and BASE is a base moiety selected from the group consisting of a pyrimidine, a purine and a deazapurine, or analog thereof, said PM being attached to SM, said BASE being attached to SM, and Sig being covalently attached to PM directly or through a chemical linkage, said Sig comprising a non-polypeptide, non-radioactive label moiety which can be directly or indirectly detected when attached to PM or when said modified nucleotide is incorporated into said oligo- or polydeoxyribonucleotide or when said oligo- or polydeoxyribonucleotide is hybridized to said complementary nucleic acid of interest or a portion thereof.

577. The oligo- or polydeoxyribonucleotide of claim 576, wherein said Sig is or renders the nucleotide or the oligo- or polydeoxyribonucleotide self-signaling or self-indicating or self-detecting.

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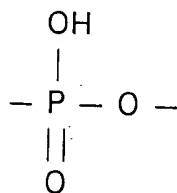
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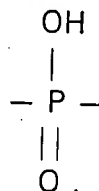
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²
~~578~~. The oligo- or polydeoxyribonucleotide of claim ~~576~~¹, wherein said Sig moiety comprises at least three carbon atoms.

³
~~579~~. The oligo- or polydeoxyribonucleotide of claim ~~576~~¹, wherein said covalent attachment is selected from the group consisting of



and



⁴
~~580~~. The oligo- or polydeoxyribonucleotide of claim ~~576~~¹, wherein said chemical linkage does not interfere substantially with the characteristic ability of Sig to form a detectable signal.

SUB
D¹
~~581~~. The oligo- or polydeoxyribonucleotide of claim 576, wherein said chemical linkage comprises a member selected from the group consisting of an olefinic bond at the α -position relative to the point of attachment to the nucleotide, a $-\text{CH}_2\text{NH}-$ moiety, or both.

⁶
~~582~~. The oligo- or polydeoxyribonucleotide of claim ~~576~~¹, wherein said chemical linkage comprises an allylamine group.

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$$-S-, \overset{\overset{O}{\parallel}}{-C}-O, \text{ and } -O-$$

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¹²
~~588~~. The oligo- or polydeoxyribonucleotide of claim ~~586~~¹⁰, wherein said magnetic component comprises magnetic oxide.

¹³
~~589~~. The oligo- or polydeoxyribonucleotide of claim ~~588~~¹², wherein said magnetic oxide comprises ferric oxide.

N¹
C004.
¹⁴
~~590~~. The oligo- or polydeoxyribonucleotide of claim ~~586~~¹⁰, wherein said metal-containing component is catalytic.

¹⁵
~~591~~. The oligo- or polydeoxyribonucleotide of claim ~~586~~¹⁰, wherein said fluorescent component comprises a member selected from the group consisting of fluorescein, rhodamine and dansyl.

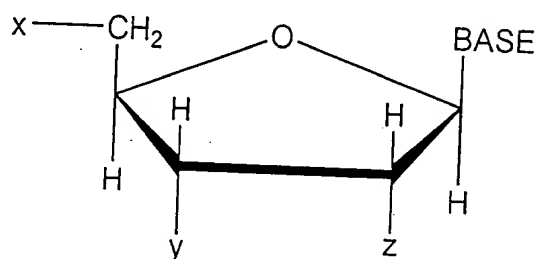
¹⁶
~~592~~. The oligo- or polydeoxyribonucleotide of claim ~~576~~¹, wherein said Sig moiety is attached to a terminal nucleotide in said oligo- or polydeoxyribonucleotide.

¹⁷
~~593~~. The oligo- or polydeoxyribonucleotide of claim ~~592~~¹⁶, wherein the sugar moiety of said terminal nucleotide has a hydrogen atom at the 2' position thereof.

¹⁸
~~594~~. The oligo- or polydeoxyribonucleotide of claim ~~592~~¹⁶, wherein the sugar moiety of said terminal nucleotide has oxygen atoms at each of the 2' and 3' positions thereof.

¹⁹
~~595~~. The oligo- or polydeoxyribonucleotide of claim ~~576~~¹, comprising at least one ribonucleotide.

20
586. An oligo- or polydeoxyribonucleotide which is complementary to a nucleic acid of interest or a portion thereof, said oligo- or polydeoxyribonucleotide comprising at least one modified nucleotide having the structural formula:



N¹
CDU-4.
wherein BASE is a moiety selected from the group consisting of a pyrimidine, a purine and a deazapurine, or analog thereof, and wherein BASE is attached to the 1' position of the pentose ring from the N1 position when BASE is a pyrimidine or from the N9 position when BASE is a purine or a deazapurine;

wherein x is selected from the group consisting of H—, HO—, a mono-phosphate, a di-phosphate and a tri-phosphate;

wherein y is selected from the group consisting of H—, HO—, a mono-phosphate, a di-phosphate and a tri-phosphate;

wherein z is selected from the group consisting of H—, HO—, a mono-phosphate, a di-phosphate and a tri-phosphate; and

wherein Sig is covalently attached directly or through a chemical linkage to at least one phosphate selected from the group consisting of x, y, z, and a combination thereof, said Sig comprising a non-polypeptide, non-radioactive label moiety which can be directly or indirectly detected when so attached to said phosphate or when said modified nucleotide is incorporated into said oligo- or polydeoxyribonucleotide or when said oligo- or polydeoxyribonucleotide is hybridized to said complementary nucleic acid of interest or a portion thereof.

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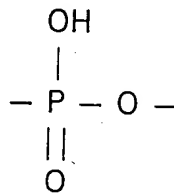
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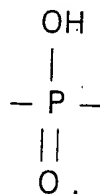
597. The oligo- or polydeoxyribonucleotide of claim 596, wherein said Sig is or renders the nucleotide or the oligo- or polydeoxyribonucleotide self-signaling or self-indicating or self-detecting.

598. The oligo- or polydeoxyribonucleotide of claim 596, wherein said Sig moiety comprises at least three carbon atoms.

599. The oligo- or polydeoxyribonucleotide of claim 596, wherein said covalent attachment is selected from the group consisting of



and



600. The oligo- or polydeoxyribonucleotide of claim 596, wherein said chemical linkage does not interfere substantially with the characteristic ability of Sig to form a detectable signal.

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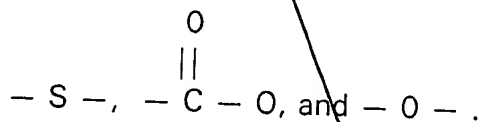
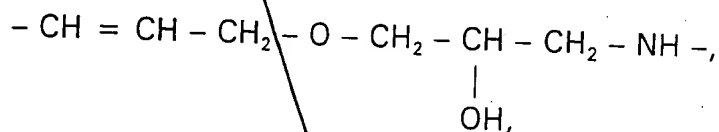
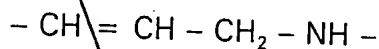
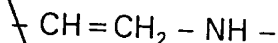
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SUB
03
601. The oligo- or polydeoxyribonucleotide of claim 596, wherein said chemical linkage comprises a member selected from the group consisting of an olefinic bond at the α -position relative to the point of attachment to the nucleotide, a $-\text{CH}_2\text{NH}-$ moiety, or both.

25
20
602. The oligo- or polydeoxyribonucleotide of claim 596, wherein said chemical linkage comprises an allylamine group.

N'
COND.
603. The oligo- or polydeoxyribonucleotide of claim 596, wherein said chemical linkage comprises or includes an olefinic bond at the α -position relative to the point of attachment to x, y or z, or any of the moieties:



27
20
604. The oligo- or polydeoxyribonucleotide of claim 596, wherein said chemical linkage of Sig includes a glycosidic linkage moiety.

28
20
605. The oligo- or polydeoxyribonucleotide of claim 596, wherein said x and y each comprise a member selected from the group consisting of a monophosphate, a diphosphate and a triphosphate and said Sig moiety is covalently attached to either or both of said x and y through a phosphorus atom or phosphate oxygen.

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²⁹
~~606~~. The oligo- or polydeoxyribonucleotide of claim ~~596~~²⁹, wherein Sig comprises a component selected from the group consisting of biotin, iminobiotin, an electron dense component, a magnetic component, a metal-containing component, a fluorescent component, a chemiluminescent component, a chromogenic component or a combination of any of the foregoing.

³⁰
~~607~~. The oligo- or polydeoxyribonucleotide of claim ~~606~~²⁹, wherein said electron dense component comprises ferritin.

N¹
cont.
³¹
~~608~~. The oligo- or polydeoxyribonucleotide of claim ~~606~~²⁹, wherein said magnetic component comprises magnetic oxide.

³²
~~609~~. The oligo- or polydeoxyribonucleotide of claim ~~608~~³¹, wherein said magnetic oxide comprises ferric oxide.

³³
~~610~~. The oligo- or polydeoxyribonucleotide of claim ~~606~~²⁹, wherein said metal-containing component is catalytic.

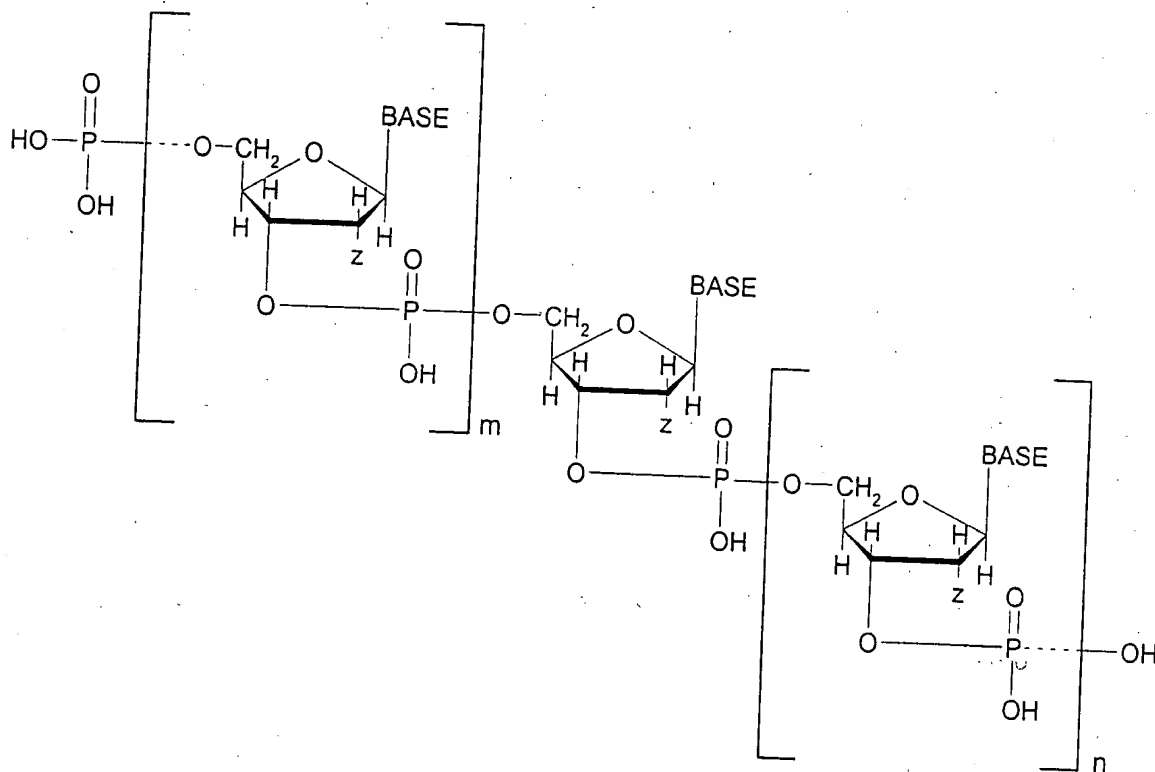
³⁴
~~611~~. The oligo- or polydeoxyribonucleotide of claim ~~606~~²⁹, wherein said fluorescent component comprises a member selected from the group consisting of fluorescein, rhodamine and dansyl.

³⁵
~~612~~. The oligo- or polydeoxyribonucleotide of claim ~~596~~²⁰, wherein said Sig moiety is attached to a terminal nucleotide in said oligo- or polydeoxyribonucleotide.

~~614~~³⁷. The oligo- or polydeoxyribonucleotide of claim ~~612~~³⁵, wherein both y and z of said terminal nucleotide comprise an oxygen atom at each of the 3' and 2' positions thereof, respectively.

~~38~~
615. The oligo- or polydeoxyribonucleotide of claim ~~596~~²⁰, comprising at least one ribonucleotide.

³⁹
~~616~~. The oligo- or polydexoyribonucleotide of claim ~~596~~²⁰, having the structural formula:



wherein m and n represent integers from 0 up to about 100,000, and wherein said Sig. moiety is attached to at least one of the phosphate moieties in said structural formula.

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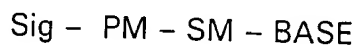
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40

617. An oligo- or polynucleotide which is complementary to a nucleic acid of interest or a portion thereof, said oligo- or polynucleotide comprising at least one modified nucleotide having the formula



N¹
cont.

wherein PM is a phosphate moiety, SM is a sugar moiety and BASE is a moiety selected from the group consisting of a pyrimidine, a purine and a deazapurine, or analog thereof, said PM being attached to SM, said BASE being attached to SM, and Sig being covalently attached to PM directly or via a chemical linkage, said Sig comprising a non-polypeptide, non-radioactive label moiety which can be directly or indirectly detected when attached to PM or when said modified nucleotide is incorporated into said oligo- or polynucleotide, or when said oligo- or polynucleotide is hybridized to said complementary nucleic acid of interest or a portion thereof, provided that when said oligo- or polynucleotide is an oligoribonucleotide or a polyribonucleotide, and when Sig is attached through a chemical linkage to a terminal PM at the 3' position of a terminal ribonucleotide, said chemical linkage is not obtained through a 2',3' vicinal oxidation of a 3' terminal ribonucleotide previously attached to said oligoribonucleotide or polyribonucleotide.

618. The oligo- or polynucleotide of claim 617, wherein said Sig is or renders the nucleotide or the oligo- or polynucleotide self-signaling or self-indicating or self-detecting.

41

619. The oligo- or polynucleotide of claim 617, wherein said Sig moiety comprises at least three carbon atoms.

40

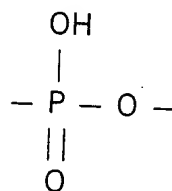
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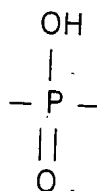
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42/ 620. The oligo- or polynucleotide of claim ~~617~~⁴⁰, wherein said covalent attachment is selected from the group consisting of



and



43/ 621. The oligo- or polynucleotide of claim ~~617~~⁴⁰, wherein said chemical linkage does not interfere substantially with the characteristic ability of Sig to form a detectable signal.

SUB 05 622. The oligo- or polynucleotide of claim 617, wherein said chemical linkage comprises a member selected from the group consisting of an olefinic bond at the α -position relative to the point of attachment to the nucleotide, a $-\text{CH}_2\text{NH}-$ moiety, or both.

45/ 623. The oligo- or polynucleotide of claim ~~617~~⁴⁰, wherein said chemical linkage comprises an allylamine group.

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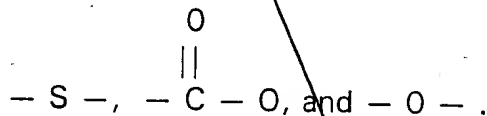
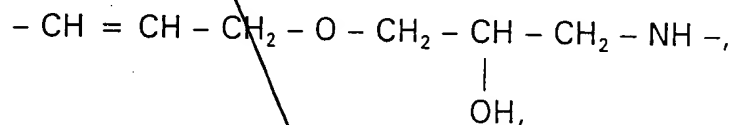
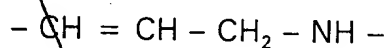
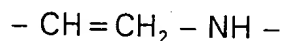
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SUB
D6

N'
CONT.

624. The oligo- or polynucleotide of claim 617, wherein said chemical linkage comprises or includes an olefinic bond at the α -position relative to the point of attachment to the nucleotide, or any of the moieties:



47

625. The oligo- or polynucleotide of claim 617, wherein said chemical linkage of Sig includes a glycosidic linkage moiety.

48

40

626. The oligo- or polynucleotide of claim 617, wherein said PM is a monophosphate, a diphosphate or a triphosphate and said Sig moiety is covalently attached to said PM through a phosphorus atom or a phosphate oxygen.

49

40

627. The oligo- or polynucleotide of claim 617, wherein Sig comprises a component selected from the group consisting of biotin, iminobiotin, an electron dense component, a magnetic component, a metal-containing component, a fluorescent component, a chemiluminescent component, a chromogenic component or a combination of any of the foregoing.

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~~50~~ 628. The oligo- or polynucleotide of claim ~~49~~ 627, wherein said electron dense component comprises ferritin.

~~51~~ 629. The oligo- or polynucleotide of claim ~~49~~ 627, wherein said magnetic component comprises magnetic oxide.

~~52~~ 630. The oligo- or polynucleotide of claim ~~51~~ 629, wherein said magnetic oxide comprises ferric oxide.

N¹
CONT. ~~53~~ 631. The oligo- or polynucleotide of claim ~~49~~ 627, wherein said metal-containing component is catalytic.

~~54~~ 632. The oligo- or polynucleotide of claim ~~49~~ 627, wherein said fluorescent component comprises a member selected from the group consisting of fluorescein, rhodamine and dansyl.

~~55~~ 633. The oligo- or polynucleotide of claim ~~40~~ 617, wherein said Sig moiety is attached to a terminal nucleotide in said oligo- or polynucleotide.

~~56~~ 634. The oligo- or polynucleotide of claim ~~55~~ 633, wherein the sugar moiety of said terminal nucleotide has a hydrogen atom at the 2' position thereof.

~~57~~ 635. The oligo- or polynucleotide of claim ~~55~~ 633, wherein the sugar moiety of said terminal nucleotide has an oxygen atom at each of the 2' and 3' positions thereof.

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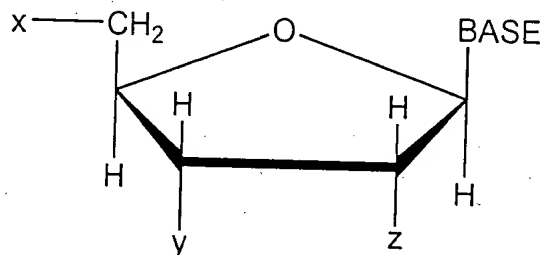
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⁵⁸
~~636~~. The oligo- or polynucleotide of claim ⁴⁷~~617~~, comprising at least one deoxyribonucleotide.

⁵⁹
~~637~~. An oligo- or polynucleotide which is complementary to a nucleic acid of interest or a portion thereof, said oligo- or polynucleotide comprising at least one modified nucleotide having the structural formula:



wherein BASE is a moiety selected from the group consisting of a pyrimidine, a purine and a deazapurine, or analog thereof, and wherein BASE is attached to the 1' position of the pentose ring from the N1 position when BASE is a pyrimidine or from the N9 position when BASE is a purine or a deazapurine;

wherein x is selected from the group consisting of H—, HO—, a mono-phosphate, a di-phosphate and a tri-phosphate;

wherein y is selected from the group consisting of H—, HO—, a mono-phosphate, a di-phosphate and a tri-phosphate;

wherein z is selected from the group consisting of H—, HO—, a mono-phosphate, a di-phosphate and a tri-phosphate; and

wherein Sig is covalently attached directly or through a chemical linkage to at least one phosphate selected from the group consisting of x, y and z, and a combination thereof, said Sig comprising a non-polypeptide, non-radioactive label moiety which can be directly or indirectly detected when so attached to said

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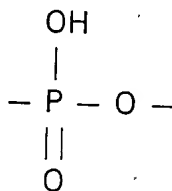
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N¹
C804
phosphate or when said modified nucleotide is incorporated into said oligo- or polynucleotide, or when said oligo- or polynucleotide is hybridized to said complementary nucleic acid of interest or a portion thereof, provided that when said oligo- or polynucleotide is an oligoribonucleotide or a polyribonucleotide and when Sig is attached through a chemical linkage to a terminal PM at the 3' position of a terminal ribonucleotide, said chemical linkage is not obtained through a 2',3' vicinal oxidation of a 3' terminal ribonucleotide previously attached to said oligoribonucleotide or polyribonucleotide.

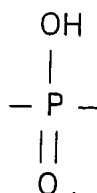
638. The oligo- or polynucleotide of claim 637, wherein said Sig is or renders the nucleotide or the oligo- or polynucleotide self-signaling or self-indicating or self-detecting.

60
639. The oligo- or polynucleotide of claim 59, wherein said Sig moiety comprises at least three carbon atoms.

61
640. The oligo- or polynucleotide of claim 59, wherein said covalent attachment is selected from the group consisting of



and



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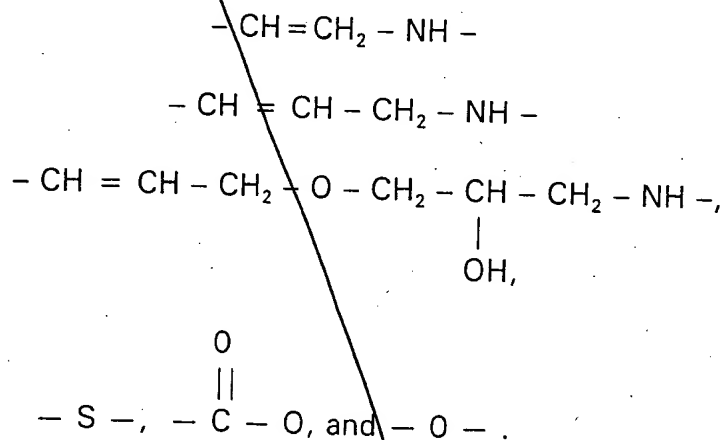
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⁶²
~~641.~~ The oligo- or polynucleotide of claim ~~637~~⁵⁹, wherein said chemical linkage does not interfere substantially with the characteristic ability of Sig to form a detectable signal.

SUB
07 → 642. The oligo- or polynucleotide of claim 637, wherein said chemical linkage comprises a member selected from the group consisting of an olefinic bond at the α -position relative to the point of attachment to the nucleotide, a $-\text{CH}_2\text{NH}-$ moiety, or both.

N¹
COOH ⁶⁴
~~643.~~ The oligo- or polynucleotide of claim ~~637~~⁵⁹, wherein said chemical linkage comprises an allylamine group.

644. The oligo- or polynucleotide of claim 637, wherein said chemical linkage comprises or includes an olefinic bond at the α -position relative to x, y or z, or any of the moieties:



⁶⁶
~~645.~~ The oligo- or polynucleotide of claim ~~637~~⁵⁹, wherein said chemical linkage of Sig includes a glycosidic linkage moiety.

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⁶⁷
~~646~~. The oligo- or polynucleotide of claim ~~637~~⁵⁹, wherein said x and y each
comprise a member selected from the group consisting of a monophosphate, a
diphosphate and a triphosphate and Sig moiety is covalently attached to either or
both of said x and y through a phosphorus atom or a phosphate oxygen.

⁶⁸
~~647~~. The oligo- or polynucleotide of claim ~~637~~⁵⁹, wherein Sig comprises a
component selected from the group consisting of biotin, iminobiotin, an electron
dense component, a magnetic component, a metal-containing component, a
fluorescent component, a chemiluminescent component, a chromogenic component
or a combination of any of the foregoing.

⁶⁹
~~648~~. The oligo- or polynucleotide of claim ~~647~~⁶⁸, wherein said electron dense
component comprises ferritin.

⁷⁰
~~649~~. The oligo- or polynucleotide of claim ~~647~~⁶⁸, wherein said magnetic component
comprises magnetic oxide.

⁷¹
~~650~~. The oligo- or polynucleotide of claim ~~649~~⁷⁰, wherein said magnetic oxide
comprises ferric oxide.

⁷²
~~651~~. The oligo- or polynucleotide of claim ~~647~~⁶⁸, wherein said metal-containing
component is catalytic.

⁷³
~~652~~. The oligo- or polynucleotide of claim ~~647~~⁶⁸, wherein said fluorescent
component comprises a member selected from the group consisting of fluorescein,
rhodamine and dansyl.

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⁷⁴
~~653~~. The oligo- or polynucleotide of claim ~~637~~⁵⁹, wherein said Sig moiety is
attached to a terminal nucleotide in said oligo- or polynucleotide.

⁷⁵
~~654~~. The oligo- or polynucleotide of claim ~~653~~⁷⁴, wherein z of said terminal
nucleotide comprises a hydrogen atom at the 2' position thereof.

⁷⁶
~~655~~. The oligo- or polynucleotide of claim ~~653~~⁷⁴, wherein both y and z of said
terminal nucleotide comprise an oxygen atom at each of the 3' and 2'
positions thereof, respectively.

⁷⁷
~~656~~. The oligo- or polynucleotide of claim ~~637~~⁵⁹, comprising at least one
deoxyribonucleotide.

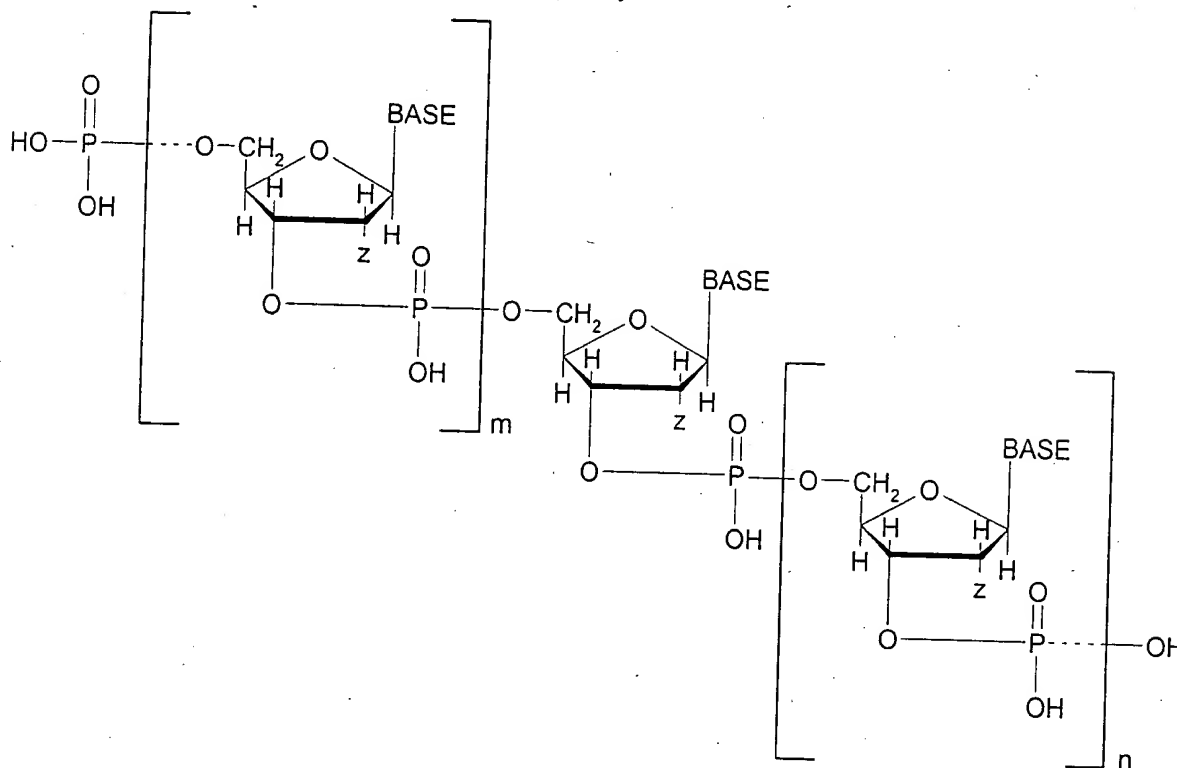
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⁷⁸
~~657~~. The oligo- or polynucleotide of claim ⁵⁹~~637~~, having the structural formula:



wherein m and n represent integers from 0 up to about 100,000, and wherein said Sig moiety is attached to at least one of the phosphate moieties in said structural formula.

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658. An oligo- or polydeoxyribonucleotide which is complementary to a nucleic acid of interest or a portion thereof, said oligo- or polydeoxyribonucleotide comprising at least one modified nucleotide having the formula

Sig-PM-SM-BASE

N¹
const

wherein PM is a phosphate moiety, SM is a sugar moiety and BASE is a base moiety selected from the group consisting of a pyrimidine, a purine and a deazapurine, or analog thereof, said PM being attached to SM, said BASE being attached to SM, and Sig being covalently attached to PM directly or through a chemical linkage, said Sig comprising a non-radioactive label moiety which can be directly or indirectly detected when attached to PM or when said modified nucleotide is incorporated into said oligo- or polydeoxyribonucleotide or when said oligo- or polydeoxyribonucleotide is hybridized to said complementary nucleic acid of interest or a portion thereof, and wherein Sig comprises biotin, iminobiotin, an electron dense component, a magnetic component, a metal-containing component, a fluorescent component, a chemiluminescent component, a chromogenic component or a combination of any of the foregoing.

659. The oligo- or polydeoxyribonucleotide of claim 658, wherein said Sig is or renders the nucleotide or the oligo- or polydeoxyribonucleotide self-signaling or self-indicating or self-detecting.

80

660. The oligo- or polydeoxyribonucleotide of claim 658, wherein said Sig moiety comprises at least three carbon atoms.

79

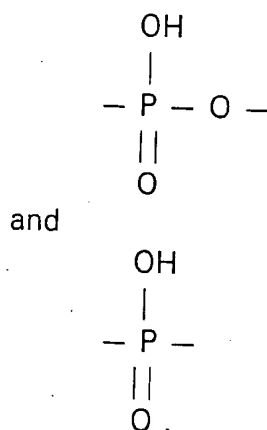
Dean L. Engelhardt, et al.

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~~81~~ 79
661. The oligo- or polydeoxyribonucleotide of claim ~~658~~, wherein said covalent attachment is selected from the group consisting of



N¹
CD¹⁵⁴
~~82~~ 79
662. The oligo- or polydeoxyribonucleotide of claim ~~658~~, wherein said chemical linkage does not interfere substantially with the characteristic ability of Sig to form a detectable signal.

SUB
09
~~83~~
663. The oligo- or polydeoxyribonucleotide of claim ~~658~~, wherein said chemical linkage comprises a member selected from the group consisting of an olefinic bond at the α -position relative to the point of attachment to the nucleotide, a -CH₂NH- moiety, or both.

~~84~~ 79
664. The oligo- or polydeoxyribonucleotide of claim ~~658~~, wherein said chemical linkage comprises an allylamine group.

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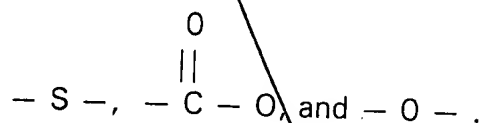
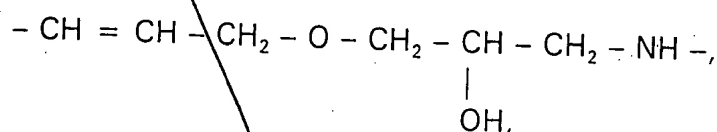
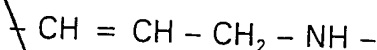
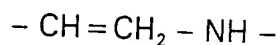
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SUB
610

665. The oligo- or polydeoxyribonucleotide of claim 658, wherein said chemical linkage comprises or includes an olefinic bond at the α -position relative to the point of attachment to the nucleotide, or any of the moieties:



86
666. The oligo- or polydeoxyribonucleotide of claim 658, wherein said chemical linkage of Sig includes a glycosidic linkage moiety. 79

87
667. The oligo- or polydeoxyribonucleotide of claim 658, wherein said PM is monophosphate, a diphosphate or a triphosphate and said Sig moiety is covalently attached to said PM through a phosphorus atom or phosphate oxygen. 79

88
668. The oligo- or polydeoxyribonucleotide of claim 658, wherein said electron dense component comprises ferritin. 79

89
669. The oligo- or polydeoxyribonucleotide of claim 658, wherein said magnetic component comprises magnetic oxide. 79

90
670. The oligo- or polydeoxyribonucleotide of claim 658, wherein said magnetic oxide comprises ferric oxide. 79

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~~91~~ ~~79~~
~~671~~. The oligo- or polydeoxyribonucleotide of claim ~~658~~, wherein said metal-containing component is catalytic.

~~92~~ ~~79~~
~~672~~. The oligo- or polydeoxyribonucleotide of claim ~~658~~, wherein said fluorescent component comprises a member selected from the group consisting of fluorescein, rhodamine and dansyl.

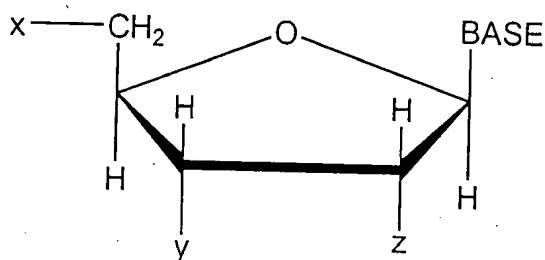
~~93~~ ~~79~~
~~673~~. The oligo- or polydeoxyribonucleotide of claim ~~658~~, wherein said Sig moiety is attached to a terminal nucleotide in said oligo- or polydeoxyribonucleotide.

N¹
CDS⁴
~~94~~ ~~93~~
~~674~~. The oligo- or polydeoxyribonucleotide of claim ~~673~~, wherein the sugar moiety of said terminal nucleotide has a hydrogen atom at the 2' position thereof.

~~95~~ ~~93~~
~~675~~. The oligo- or polydeoxyribonucleotide of claim ~~673~~, wherein the sugar moiety of said terminal nucleotide has oxygen atoms at each of the 2' and 3' positions thereof.

~~96~~ ~~79~~
~~676~~. The oligo- or polydeoxyribonucleotide of claim ~~658~~, comprising at least one ribonucleotide.

97
677. An oligo- or polydeoxyribonucleotide which is complementary to a nucleic acid of interest or a portion thereof, said oligo- or polydeoxyribonucleotide comprising at least one modified nucleotide having the structural formula:



N¹
cost.
wherein BASE is a moiety selected from the group consisting of a pyrimidine, a purine and a deazapurine, or analog thereof, and wherein BASE is attached to the 1' position of the pentose ring from the N1 position when BASE is a pyrimidine or from the N9 position when BASE is a purine or a deazapurine;

wherein x is selected from the group consisting of H—, HO—, a mono-phosphate, a di-phosphate and a tri-phosphate;

wherein y is selected from the group consisting of H—, HO—, a mono-phosphate, a di-phosphate and a tri-phosphate;

wherein z is selected from the group consisting of H—, HO—, a mono-phosphate, a di-phosphate and a tri-phosphate; and

wherein Sig is covalently attached directly or through a chemical linkage to at least one phosphate selected from the group consisting of x, y, z, and a combination thereof, said Sig comprising a non-radioactive label moiety which can be directly or indirectly detected when so attached to said phosphate or when said modified nucleotide is incorporated into said oligo- or polydeoxyribonucleotide or when said oligo- or polydeoxyribonucleotide is hybridized to said complementary nucleic acid of interest or a portion thereof, wherein Sig comprises biotin,

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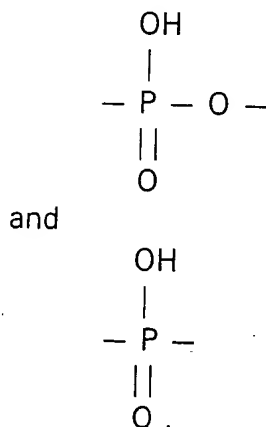
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iminobiotin, an electron dense component, a magnetic component, a metal-containing component, a fluorescent component, a chemiluminescent component, a chromogenic component or a combination of any of the foregoing.

678. The oligo- or polydeoxyribonucleotide of claim 677, wherein said Sig is or renders the nucleotide or the oligo- or polydeoxyribonucleotide self-signaling or self-indicating or self-detecting.

98
N¹ 679. The oligo- or polydeoxyribonucleotide of claim 677, wherein said Sig moiety comprises at least three carbon atoms.

99
680. The oligo- or polydeoxyribonucleotide of claim 677, wherein said covalent attachment is selected from the group consisting of



100
681. The oligo- or polydeoxyribonucleotide of claim 677, wherein said chemical linkage does not interfere substantially with the characteristic ability of Sig to form a detectable signal.

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SUB
011

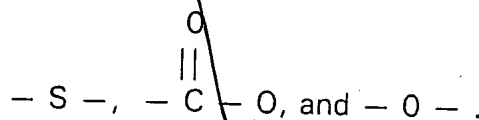
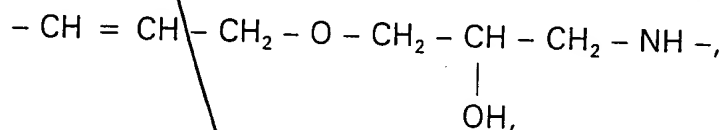
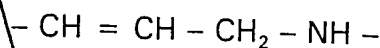
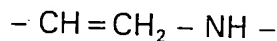
682. The oligo- or polydeoxyribonucleotide of claim 677, wherein said chemical linkage comprises a member selected from the group consisting of an olefinic bond at the α -position relative to the point of attachment to the nucleotide, a $-\text{CH}_2\text{NH}-$ moiety, or both.

102 97

683. The oligo- or polydeoxyribonucleotide of claim 677, wherein said chemical linkage comprises an allylamine group.

N'
COO⁺

684. The oligo- or polydeoxyribonucleotide of claim 677, wherein said chemical linkage comprises or includes an olefinic bond at the α -position relative to the point of attachment to x, y or z, or any of the moieties:



104 97

685. The oligo- or polydeoxyribonucleotide of claim 677, wherein said chemical linkage of Sig includes a glycosidic linkage moiety.

105 97

686. The oligo- or polydeoxyribonucleotide of claim 677, wherein said x and y each comprise a member selected from the group consisting of a monophosphate, a diphosphate and a triphosphate and said Sig moiety is covalently attached to either or both of said x and y through a phosphorus atom or phosphate oxygen.

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¹⁰⁶
~~687~~. The oligo- or polydeoxyribonucleotide of claim ~~677~~⁹⁷, wherein said electron dense component comprises ferritin.

¹⁰⁷
~~688~~. The oligo- or polydeoxyribonucleotide of claim ~~677~~⁹⁷, wherein said magnetic component comprises magnetic oxide.

N¹
CD 44.
¹⁰⁸
~~689~~. The oligo- or polydeoxyribonucleotide of claim ~~688~~¹⁰⁷, wherein said magnetic oxide comprises ferric oxide.

¹⁰⁹
~~690~~. The oligo- or polydeoxyribonucleotide of claim ~~677~~⁹⁷, wherein said metal-containing component is catalytic.

¹¹⁰
~~691~~. The oligo- or polydeoxyribonucleotide of claim ~~677~~⁹⁷, wherein said fluorescent component comprises a member selected from the group consisting of fluorescein, rhodamine and dansyl.

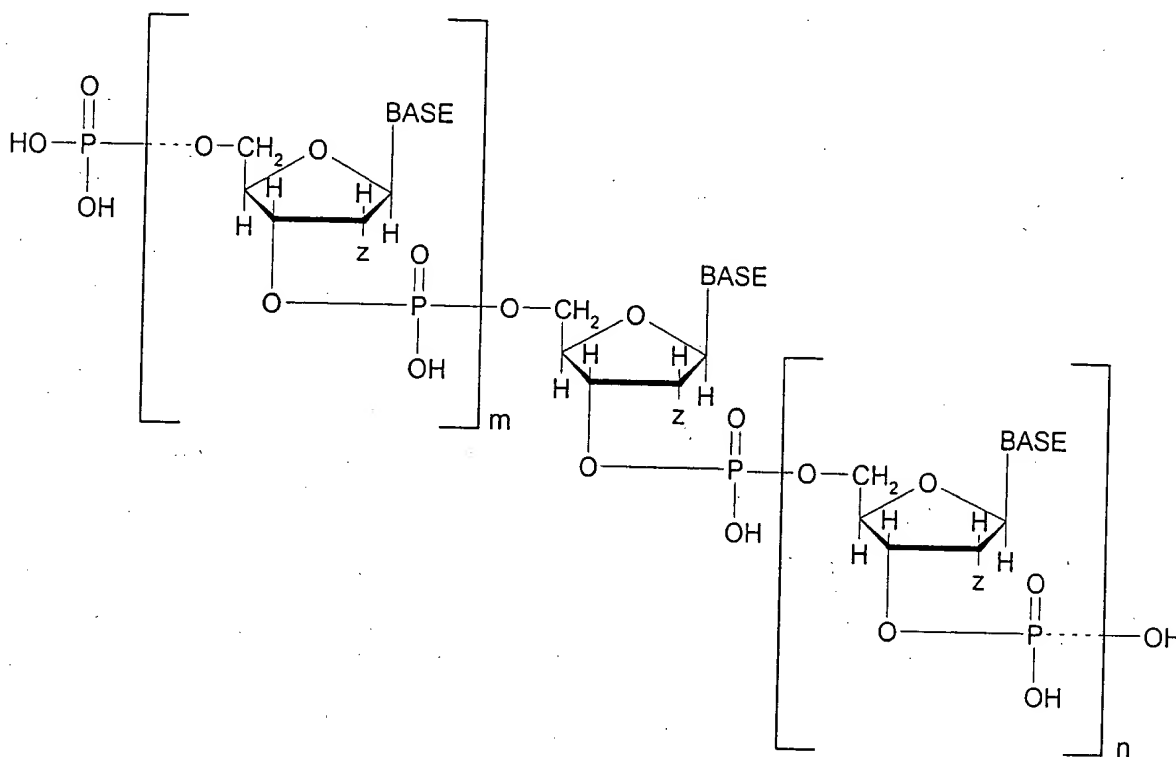
¹¹¹
~~692~~. The oligo- or polydeoxyribonucleotide of claim ~~677~~⁹⁷, wherein said Sig moiety is attached to a terminal nucleotide in said oligo- or polydeoxyribonucleotide.

¹¹²
~~693~~. The oligo- or polydeoxyribonucleotide of claim ~~692~~¹¹¹, wherein z of said terminal nucleotide comprises a hydrogen atom at the 2' position thereof.

¹¹³
~~694~~. The oligo- or polydeoxyribonucleotide of claim ~~692~~¹¹¹, wherein both y and z of said terminal nucleotide comprise an oxygen atom at each of the 3' and 2' positions thereof, respectively.

97

97



Enz-5(D6)(C2)

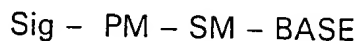
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116
~~697~~. An oligo- or polynucleotide which is complementary to a nucleic acid of interest or a portion thereof, said oligo- or polynucleotide comprising at least one modified nucleotide having the formula



NI
CON 4

wherein PM is a phosphate moiety, SM is a sugar moiety and BASE is a moiety selected from the group consisting of a pyrimidine, a purine and a deazapurine, or analog thereof, said PM being attached to SM, said BASE being attached to SM, and Sig being covalently attached to PM directly or via a chemical linkage, said Sig comprising a non-radioactive label moiety which can be directly or indirectly detected when attached to PM or when said modified nucleotide is incorporated into said oligo- or polynucleotide, or when said oligo- or polynucleotide is hybridized to said complementary nucleic acid of interest or a portion thereof, provided that when said oligo- or polynucleotide is an oligoribonucleotide or a polyribonucleotide, and when Sig is attached through a chemical linkage to a terminal PM at the 3' position of a terminal ribonucleotide, said chemical linkage is not obtained through a 2',3' vicinal oxidation of a 3' terminal ribonucleotide previously attached to said oligoribonucleotide or polyribonucleotide, wherein Sig comprises biotin, iminobiotin, an electron dense component, a magnetic component, a metal-containing component, a fluorescent component, a chemiluminescent component, a chromogenic component or a combination of any of the foregoing.

698. The oligo- or polynucleotide of claim 697, wherein said Sig is or renders the nucleotide or the oligo- or polynucleotide self-signaling or self-indicating or self-detecting.

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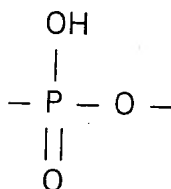
Serial No.: 08/479,997

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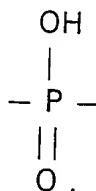
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¹¹⁷
~~699~~. The oligo- or polynucleotide of claim ~~697~~¹¹⁶, wherein said Sig moiety comprises at least three carbon atoms.

¹¹⁸
~~700~~. The oligo- or polynucleotide of claim ~~697~~¹¹⁶, wherein said covalent attachment is selected from the group consisting of



and



¹¹⁹
~~701~~. The oligo- or polynucleotide of claim ~~697~~¹¹⁶, wherein said chemical linkage does not interfere substantially with the characteristic ability of Sig to form a detectable signal.

¹²⁰
~~702~~. The oligo- or polynucleotide of claim ~~697~~¹¹⁶, wherein said chemical linkage comprises a member selected from the group consisting of an olefinic bond at the α -position relative to the point of attachment to the nucleotide, a $-\text{CH}_2\text{NH}-$ moiety, or both.

¹²¹
~~703~~. The oligo- or polynucleotide of claim ~~697~~¹¹⁶, wherein said chemical linkage comprises an allylamine group.

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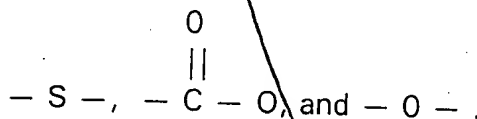
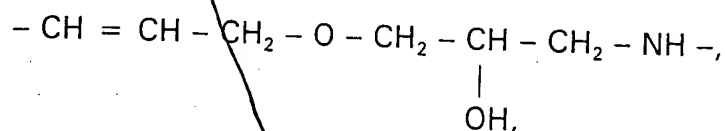
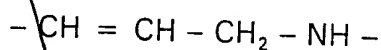
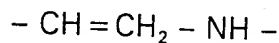
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503
014

704. The oligo- or polynucleotide of claim 697, wherein said chemical linkage comprises or includes an olefinic bond at the α -position relative to the point of attachment to the nucleotide, or any of the moieties:



123
705. The oligo- or polynucleotide of claim 697, wherein said chemical linkage of Sig includes a glycosidic linkage moiety.

124
706. The oligo- or polynucleotide of claim 697, wherein said PM is a monophosphate, a diphosphate or a triphosphate and said Sig moiety is covalently attached to said PM through a phosphorus atom or a phosphate oxygen.

125
707. The oligo- or polynucleotide of claim 697, wherein said electron dense component comprises ferritin.

126
708. The oligo- or polynucleotide of claim 697, wherein said magnetic component comprises magnetic oxide.

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¹²⁷
~~709~~. The oligo- or polynucleotide of claim ~~708~~¹²⁶, wherein said magnetic oxide comprises ferric oxide.

¹²⁸
~~710~~. The oligo- or polynucleotide of claim ~~697~~¹¹⁶, wherein said metal-containing component is catalytic.

¹²⁹
~~711~~. The oligo- or polynucleotide of claim ~~697~~¹¹⁶, wherein said fluorescent component comprises a member selected from the group consisting of fluorescein, rhodamine and dansyl.

N1
COD4. ¹³⁰
~~712~~. The oligo- or polynucleotide of claim ~~697~~¹¹⁶, wherein said Sig moiety is attached to a terminal nucleotide in said oligo- or polynucleotide.

¹³¹
~~713~~. The oligo- or polynucleotide of claim ~~712~~¹³⁰, wherein the sugar moiety of said terminal nucleotide has a hydrogen atom at the 2' position thereof.

¹³²
~~714~~. The oligo- or polynucleotide of claim ~~712~~¹³⁰, wherein the sugar moiety of said terminal nucleotide has an oxygen atom at each of the 2' and 3' positions thereof.

¹³³
~~715~~. The oligo- or polynucleotide of claim ~~697~~¹¹⁶, comprising at least one deoxyribonucleotide.

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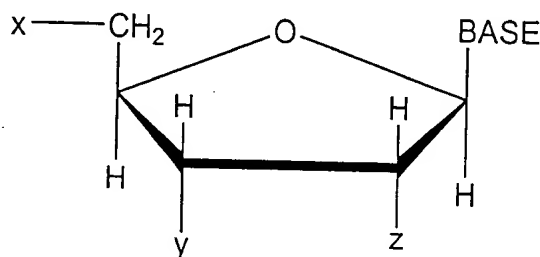
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134

716. An oligo- or polynucleotide which is complementary to a nucleic acid of interest or a portion thereof, said oligo- or polynucleotide comprising at least one modified nucleotide having the structural formula:



N¹
cont.
wherein BASE is a moiety selected from the group consisting of a pyrimidine, a purine and a deazapurine, or analog thereof, and wherein BASE is attached to the 1' position of the pentose ring from the N1 position when BASE is a pyrimidine or from the N9 position when BASE is a purine or a deazapurine;

wherein x is selected from the group consisting of H—, HO—, a mono-phosphate, a di-phosphate and a tri-phosphate;

wherein y is selected from the group consisting of H—, HO—, a mono-phosphate, a di-phosphate and a tri-phosphate;

wherein z is selected from the group consisting of H—, HO—, a mono-phosphate, a di-phosphate and a tri-phosphate; and

wherein Sig is covalently attached directly or through a chemical linkage to at least one phosphate selected from the group consisting of x, y and z, and a combination thereof, said Sig comprising a non-radioactive label moiety which can be directly or indirectly detected when so attached to said phosphate or when said modified nucleotide is incorporated into said oligo- or polynucleotide, or when said oligo- or polynucleotide is hybridized to said complementary nucleic acid of interest or a portion thereof, provided that when said oligo- or polynucleotide is an

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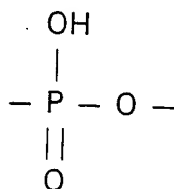
N¹
cov⁴.

oligoribonucleotide or a polyribonucleotide and when Sig is attached through a chemical linkage to a terminal PM at the 3' position of a terminal ribonucleotide, said chemical linkage is not obtained through a 2',3' vicinal oxidation of a 3' terminal ribonucleotide previously attached to said oligoribonucleotide or polyribonucleotide, wherein Sig comprises biotin, iminobiotin, an electron dense component, a magnetic component, a metal-containing component, a fluorescent component, a chemiluminescent component, a chromogenic component or a combination of any of the foregoing.

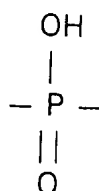
717. The oligo- or polynucleotide of claim 716, wherein said Sig is or renders the nucleotide or the oligo- or polynucleotide self-signaling or self-indicating or self-detecting.

135
718. The oligo- or polynucleotide of claim 134, wherein said Sig moiety comprises at least three carbon atoms.

136
719. The oligo- or polynucleotide of claim 134, wherein said covalent attachment is selected from the group consisting of



and



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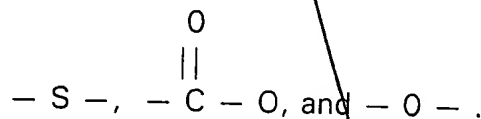
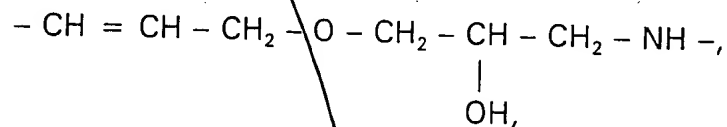
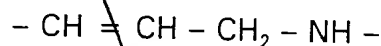
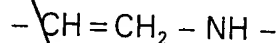
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¹³⁷
~~720.~~ The oligo- or polynucleotide of claim ~~716~~¹³⁴, wherein said chemical linkage does not interfere substantially with the characteristic ability of Sig to form a detectable signal.

SUB
DIS
N1
CONT.
721. The oligo- or polynucleotide of claim 716, wherein said chemical linkage comprises a member selected from the group consisting of an olefinic bond at the α -position relative to the point of attachment to the nucleotide, a $-\text{CH}_2\text{NH}-$ moiety, or both.

¹³⁴
~~722.~~ The oligo- or polynucleotide of claim ~~716~~¹³⁴, wherein said chemical linkage comprises an allylamine group.

723. The oligo- or polynucleotide of claim 716, wherein said chemical linkage comprises or includes an olefinic bond at the α -position relative to x, y or z, or any of the moieties:



SUB
DIS
141
~~724.~~ The oligo- or polynucleotide of claim ~~716~~¹³⁴, wherein said chemical linkage of Sig includes a glycosidic linkage moiety.

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¹⁴²
~~725~~. The oligo- or polynucleotide of claim ~~716~~¹³⁴, wherein said x and y each
comprise a member selected from the group consisting of a monophosphate, a
diphosphate and a triphosphate and Sig moiety is covalently attached to either or
both of said x and y through a phosphorus atom or a phosphate oxygen.

¹⁴³
~~726~~. The oligo- or polynucleotide of claim ~~716~~¹³⁴, wherein said electron dense
component comprises ferritin.

N!
CDUx. ¹⁴⁴
~~727~~. The oligo- or polynucleotide of claim ~~716~~¹³⁴, wherein said magnetic component
comprises magnetic oxide.

¹⁴⁵
~~728~~. The oligo- or polynucleotide of claim ~~727~~¹⁴⁴, wherein said magnetic oxide
comprises ferric oxide.

¹⁴⁶
~~729~~. The oligo- or polynucleotide of claim ~~716~~¹³⁴, wherein said metal-containing
component is catalytic.

¹⁴⁷
~~730~~. The oligo- or polynucleotide of claim ~~716~~¹³⁴, wherein said fluorescent
component comprises a member selected from the group consisting of fluorescein,
rhodamine and dansyl.

¹⁴⁸
~~731~~. The oligo- or polynucleotide of claim ~~716~~¹³⁴, wherein said Sig moiety is
attached to a terminal nucleotide in said oligo- or polynucleotide.

¹⁴⁹
~~732~~. The oligo- or polynucleotide of claim ~~731~~¹⁴⁸, wherein z of said terminal
nucleotide comprises a hydrogen atom at the 2' position thereof.

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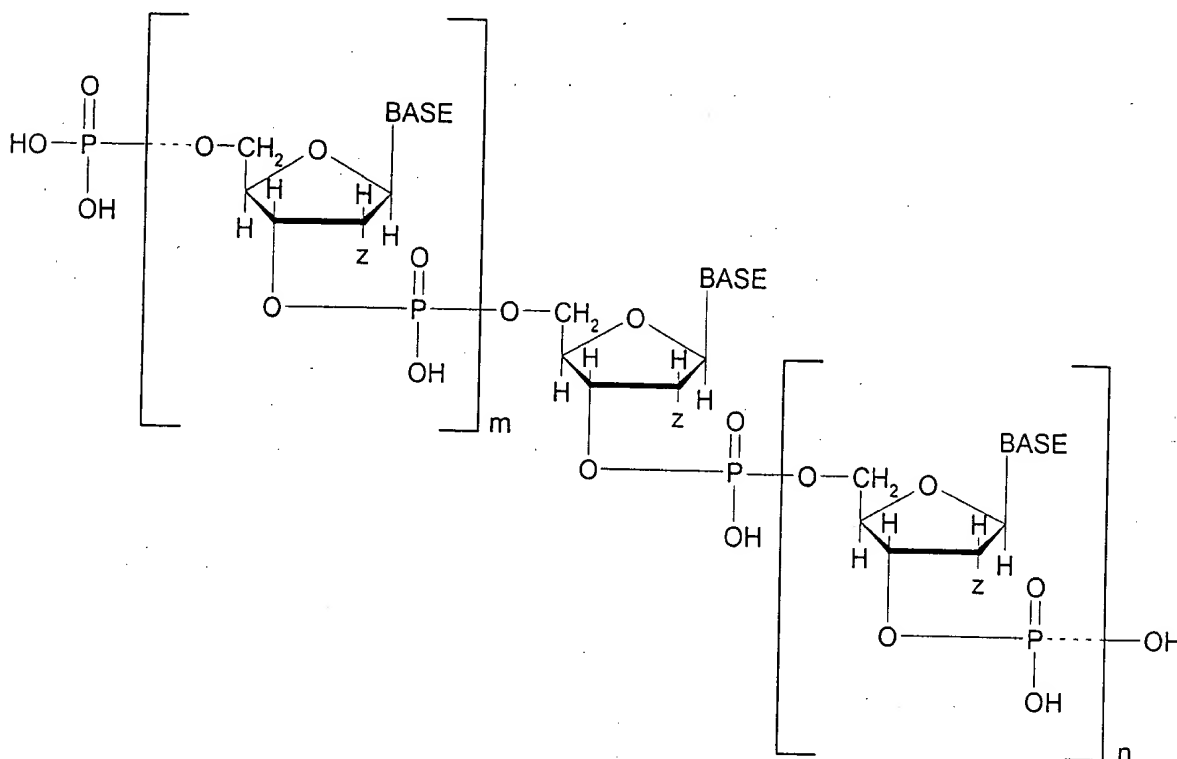
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¹⁵⁰
~~733~~. The oligo- or polynucleotide of claim ~~731~~¹⁴⁸, wherein both y and z of said terminal nucleotide comprise an oxygen atom at each of the 3' and 2' positions thereof, respectively.

¹⁶¹
~~734~~. The oligo- or polynucleotide of claim ~~716~~¹³⁴, comprising at least one deoxyribonucleotide.

¹⁵²
~~735~~. The oligo- or polynucleotide of claim ~~716~~¹³⁴, having the structural formula:



wherein m and n represent integers from 0 up to about 100,000, and wherein said Sig moiety is attached to at least one of the phosphate moieties in said structural formula.

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SUB
017

736. An oligo- or polydeoxyribonucleotide which is complementary to a nucleic acid of interest or a portion thereof, said oligo- or polydeoxyribonucleotide comprising at least one modified nucleotide having the formula

Sig-PM-SM-BASE

N¹
CON⁷

wherein PM is a phosphate moiety, SM is a sugar moiety and BASE is a base moiety selected from the group consisting of a pyrimidine, a purine and a deazapurine, or analog thereof, said PM being attached to SM, said BASE being attached to SM, and Sig being covalently attached to PM through a chemical linkage comprising a polypeptide or a protein, and said Sig comprising a non-radioactive label moiety which can be directly detected when indirectly attached to PM through said polypeptide or protein chemical linkage or when said modified nucleotide is incorporated into said oligo- or polydeoxyribonucleotide or when said oligo- or polydeoxyribonucleotide is hybridized to said complementary nucleic acid of interest or a portion thereof.

737. The oligo- or polydeoxyribonucleotide of claim 736, wherein said Sig is or renders the nucleotide or the oligo- or polydeoxyribonucleotide self-signaling or self-indicating or self-detecting.

154
738. The oligo- or polydeoxyribonucleotide of claim 153, wherein said Sig moiety comprises at least three carbon atoms.

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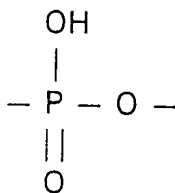
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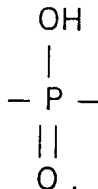
155

~~738~~. The oligo- or polydeoxyribonucleotide of claim ~~736~~, wherein said covalent attachment is selected from the group consisting of

153



and



740. The oligo- or polydeoxyribonucleotide of claim 736, wherein said polypeptide or protein chemical linkage does not interfere substantially with the characteristic ability of Sig to form a detectable signal.

741. The oligo- or polydeoxyribonucleotide of claim 736, wherein said PM is monophosphate, a diphosphate or a triphosphate and said Sig moiety is covalently attached via said polypeptide or protein chemical linkage to said PM through a phosphorus atom or phosphate oxygen.

158

~~742~~. The oligo- or polydeoxyribonucleotide of claim ~~736~~, wherein Sig comprises a component selected from the group consisting of biotin, iminobiotin, an electron dense component, a magnetic component, a metal-containing component, a fluorescent component, a chemiluminescent component, a chromogenic component or a combination of any of the foregoing.

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¹⁵⁹
~~743.~~ The oligo- or polydeoxyribonucleotide of claim ~~742~~¹⁵⁸, wherein said electron dense component comprises ferritin.

¹⁶⁰
~~744.~~ The oligo- or polydeoxyribonucleotide of claim ~~742~~¹⁵⁸, wherein said magnetic component comprises magnetic oxide.

N!
CONT.
¹⁶¹
~~745.~~ The oligo- or polydeoxyribonucleotide of claim ~~744~~¹⁶⁰, wherein said magnetic oxide comprises ferric oxide.

¹⁶²
~~746.~~ The oligo- or polydeoxyribonucleotide of claim ~~742~~¹⁵⁸, wherein said metal-containing component is catalytic.

¹⁶³
~~747.~~ The oligo- or polydeoxyribonucleotide of claim ~~742~~¹⁵⁸, wherein said fluorescent component comprises a member selected from the group consisting of fluorescein, rhodamine and dansyl.

SUB
019
~~748.~~ The oligo- or polydeoxyribonucleotide of claim 736, wherein said oligo- or polydeoxyribonucleotide is terminally ligated or attached to said polypeptide or protein chemical linkage.

¹⁶⁵
~~749.~~ The oligo- or polydeoxyribonucleotide of claim ~~736~~¹⁵³, wherein said polypeptide comprises polylysine.

¹⁶⁶
~~750.~~ The oligo- or polydeoxyribonucleotide of claim ~~736~~¹⁵³, wherein said polypeptide is selected from the group consisting of avidin, streptavidin and anti-hapten immunoglobulin.

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SUB
D20
N1
CONT.

~~751.~~ The oligo- or polydeoxyribonucleotide of claim ~~736~~, wherein said Sig moiety is attached via said polypeptide or protein chemical linkage to a phosphate moiety in a terminal nucleotide in said oligo- or polydeoxyribonucleotide.

~~168~~
~~752.~~ The oligo- or polydeoxyribonucleotide of claim ~~751~~, wherein the sugar moiety of said terminal nucleotide has a hydrogen atom at the 2' position thereof.

~~169~~
~~753.~~ The oligo- or polydeoxyribonucleotide of claim ~~751~~, wherein the sugar moiety of said terminal nucleotide has oxygen atoms at each of the 2' and 3' positions thereof.

~~170~~
~~754.~~ The oligo- or polydeoxyribonucleotide of claim ~~736~~, comprising at least one ribonucleotide.

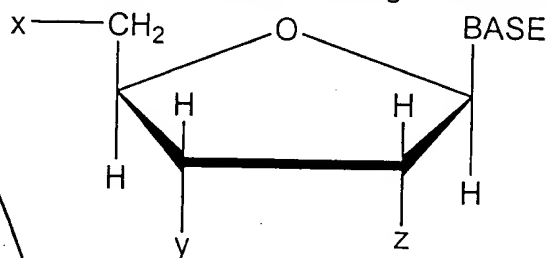
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755. An oligo- or polydeoxyribonucleotide which is complementary to a nucleic acid of interest or a portion thereof, said oligo- or polydeoxyribonucleotide comprising at least one modified nucleotide having the structural formula:



wherein BASE is a moiety selected from the group consisting of a pyrimidine, a purine and a deazapurine, or analog thereof, and wherein BASE is attached to the 1' position of the pentose ring from the N1 position when BASE is a pyrimidine or from the N9 position when BASE is a purine or a deazapurine;

wherein x is selected from the group consisting of H—, HO—, a mono-phosphate, a di-phosphate and a tri-phosphate;

wherein y is selected from the group consisting of H—, HO—, a mono-phosphate, a di-phosphate and a tri-phosphate;

wherein z is selected from the group consisting of H—, HO—, a mono-phosphate, a di-phosphate and a tri-phosphate; and

wherein Sig is covalently attached through a chemical linkage to at least one phosphate selected from the group consisting of x, y, z, and a combination thereof, said chemical linkage comprising a polypeptide or a protein, and said Sig comprising a non-radioactive label moiety which can be directly or indirectly detected when attached to said phosphate via said polypeptide or protein chemical linkage or when said modified nucleotide is incorporated into said oligo- or polydeoxynucleotide or when said oligo- or polydeoxynucleotide is hybridized to said complementary nucleic acid of interest or a portion thereof.

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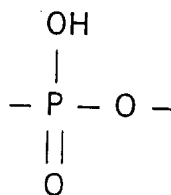
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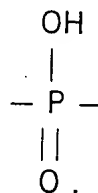
756. The oligo- or polydeoxyribonucleotide of claim 755, wherein said Sig is or renders the modified nucleotide or the oligo- or polydeoxyribonucleotide self-signaling or self-indicating or self-detecting.

757. The oligo- or polydeoxyribonucleotide of claim 755, wherein said Sig moiety comprises at least three carbon atoms.

758. The oligo- or polydeoxyribonucleotide of claim 755, wherein said covalent attachment is selected from the group consisting of



and



759. The oligo- or polydeoxyribonucleotide of claim 755, wherein said polypeptide or protein chemical linkage does not interfere substantially with the characteristic ability of Sig to form a detectable signal.

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SUB
OAA
CONT.

760. The oligo- or polydeoxyribonucleotide of claim 755, wherein said x and y each comprise a member selected from the group consisting of a monophosphate, a diphosphate and a triphosphate and said Sig moiety is covalently attached via said polypeptide or protein chemical linkage to either or both of said x and y a phosphorus atom or phosphate oxygen.

N1
CONT.

¹⁷⁶
~~761~~. The oligo- or polydeoxyribonucleotide of claim 755, wherein Sig comprises a component selected from the group consisting of biotin, iminobiotin, an electron dense component, a magnetic component, a metal-containing component, a fluorescent component, a chemiluminescent component, a chromogenic component, or a combination of any of the foregoing.

¹⁷⁷
~~762~~. The oligo- or polydeoxyribonucleotide of claim ¹⁷⁶~~761~~, wherein said electron dense component comprises ferritin.

¹⁷⁸
~~763~~. The oligo- or polydeoxyribonucleotide of claim ¹⁷⁶~~761~~, wherein said magnetic component comprises magnetic oxide.

¹⁷⁹
~~764~~. The oligo- or polydeoxyribonucleotide of claim ¹⁷⁸~~763~~, wherein said magnetic oxide comprises ferric oxide.

¹⁸⁰
~~765~~. The oligo- or polydeoxyribonucleotide of claim ¹⁷⁶~~761~~, wherein said metal-containing component is catalytic.

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¹⁴¹
~~766~~. The oligo- or polydeoxyribonucleotide of claim ~~761~~¹⁷⁶, wherein said fluorescent component comprises a member selected from the group consisting of fluorescein, rhodamine and dansyl.

SUB
D23

767. The oligo- or polydeoxyribonucleotide of claim 755, wherein said oligo- or polydeoxyribonucleotide is terminally ligated or attached to said polypeptide or protein chemical linkage.

NI
CONT.

¹⁸³
~~768~~. The composition of claim ~~755~~¹⁷¹, wherein said polypeptide comprises polylysine.

¹⁸⁴
~~769~~. The composition of claim ~~755~~¹⁷¹, wherein said polypeptide is selected from the group consisting of avidin, streptavidin and anti-hapten immunoglobulin.

SUB
D24

770. The oligo- or polydeoxyribonucleotide of claim 755, wherein said Sig moiety is attached via said polypeptide or protein chemical linkage to a terminal nucleotide in said oligo- or polydeoxyribonucleotide.

¹⁸⁶
~~771~~. The oligo- or polydeoxyribonucleotide of claim ~~770~~¹⁸⁵, wherein z of said terminal nucleotide comprises a hydrogen atom at the 2' position thereof.

¹⁸⁷
~~772~~. The oligo- or polydeoxyribonucleotide of claim ~~770~~¹⁸⁵, wherein both y and z of said terminal nucleotide comprise an oxygen atom at each of the 3' and 2' positions thereof, respectively.

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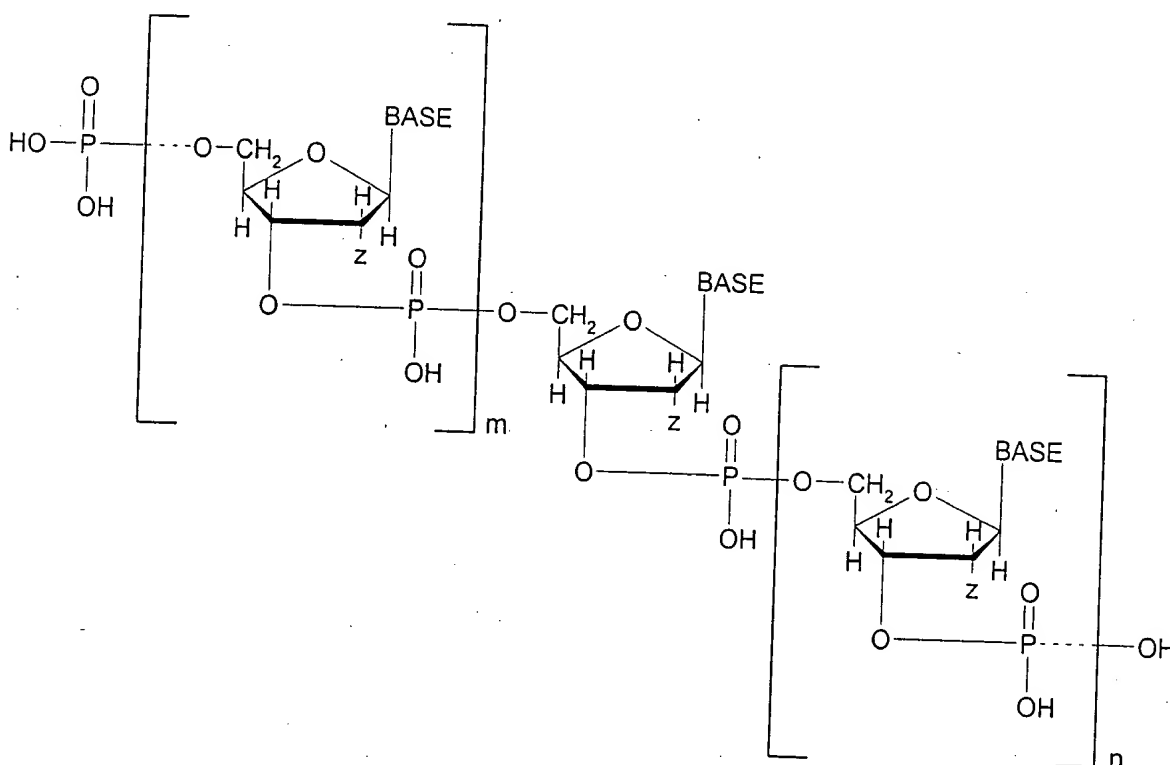
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¹⁸⁶
~~773~~. The oligo- or polydeoxyribonucleotide of claim ~~755~~¹⁷¹, comprising at least one ribonucleotide.

¹⁸⁹
~~774~~. The oligo- or polydeoxyribonucleotide of claim ~~755~~¹⁷¹, having the structural formula:



wherein m and n represent integers from 0 up to about 100,000, and wherein said Sig moiety is attached to at least one of the phosphate moieties in said structural formula.

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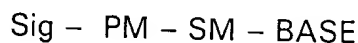
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SUB
D25

775. An oligo- or polynucleotide which is complementary to a nucleic acid of interest or a portion thereof, said oligo- or polynucleotide comprising at least one modified nucleotide having the formula



N¹
CON⁴.

wherein PM is a phosphate moiety, SM is a sugar moiety and BASE is a moiety selected from the group consisting of a pyrimidine, a purine and a deazapurine, or analog thereof, said PM being attached to SM, said BASE being attached to SM, and Sig being covalently attached to PM via a chemical linkage comprising a polypeptide or a protein, said Sig comprising a non-radioactive label moiety which can be directly or indirectly detected when attached to PM via said polypeptide or protein chemical linkage or when said modified nucleotide is incorporated into said oligo- or polynucleotide, or when said oligo- or polynucleotide is hybridized to said complementary nucleic acid of interest or a portion thereof, provided that when said oligo- or polynucleotide is an oligoribonucleotide or a polyribonucleotide, and when Sig is attached through a chemical linkage to a terminal PM at the 3' position of a terminal ribonucleotide, said chemical linkage is not obtained through a 2',3' vicinal oxidation of a 3' terminal ribonucleotide previously attached to said oligoribonucleotide or polyribonucleotide.

776. The oligo- or polynucleotide of claim 775, wherein said Sig is or renders the nucleotide or the oligo- or polynucleotide self-signaling or self-indicating or self-detecting.

191
777. The oligo- or polynucleotide of claim 191, wherein said Sig moiety comprises at least three carbon atoms.

190
775. The oligo- or polynucleotide of claim 190, wherein said Sig moiety comprises at least three carbon atoms.

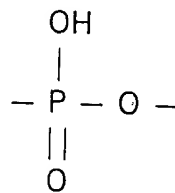
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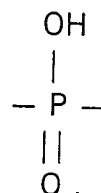
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¹⁹²
~~778~~. The oligo- or polynucleotide of claim ~~775~~¹⁹⁰, wherein said covalent attachment is selected from the group consisting of



and



¹⁹⁵
~~779~~. The oligo- or polynucleotide of claim ~~775~~¹⁹⁰, wherein said polypeptide or protein chemical linkage does not interfere substantially with the characteristic ability of Sig to form a detectable signal.

¹⁹⁶
~~780~~. The oligo- or polynucleotide of claim ~~775~~¹⁹⁰, wherein said PM is a monophosphate, a diphosphate or a triphosphate and said Sig moiety is covalently attached via said polypeptide or protein chemical linkage to said PM through a phosphorus atom or a phosphate oxygen.

¹⁹⁷
~~781~~. The oligo- or polynucleotide of claim ~~775~~¹⁹⁰, wherein Sig comprises a component selected from the group consisting of biotin, iminobiotin, an electron dense component, a magnetic component, a metal-containing component, a fluorescent component, a chemiluminescent component, a chromogenic component or a combination of any of the foregoing.

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¹⁹⁶
~~782.~~ The oligo- or polynucleotide of claim ~~781~~¹⁹⁵, wherein said electron dense component comprises ferritin.

¹⁴⁷
~~783.~~ The oligo- or polynucleotide of claim ~~781~~¹⁹⁵, wherein said magnetic component comprises magnetic oxide.

¹⁹⁸
~~784.~~ The oligo- or polynucleotide of claim ~~783~~¹⁹⁷, wherein said magnetic oxide comprises ferric oxide.

¹⁹⁹
~~785.~~ The oligo- or polynucleotide of claim ~~781~~¹⁹⁵, wherein said metal-containing component is catalytic.

²⁰⁰
~~786.~~ The oligo- or polynucleotide of claim ~~781~~¹⁹⁵, wherein said fluorescent component comprises a member selected from the group consisting of fluorescein, rhodamine and dansyl.

~~787.~~ The oligo- or polynucleotide of claim 775, wherein said oligo- or polynucleotide is terminally ligated or attached to said polypeptide or protein chemical linkage.

²⁰²
~~788.~~ The oligo- or polynucleotide of claim ~~775~~¹⁹⁰, wherein said polypeptide comprises polylysine.

²⁰³
~~789.~~ The oligo- or polynucleotide of claim ~~775~~¹⁹⁰, wherein said polypeptide is selected from the group consisting of avidin, streptavidin and anti-hapten immunoglobulin.

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SW3
028
N¹
COU¹.

790. The oligo- or polynucleotide of claim 775, wherein said Sig moiety is attached via said polypeptide or protein chemical linkage to a terminal nucleotide in said oligo- or polynucleotide.

205
204
791. The oligo- or polynucleotide of claim ~~790~~, wherein the sugar moiety of said terminal nucleotide has a hydrogen atom at the 2' position thereof.

206
204
792. The oligo- or polynucleotide of claim ~~790~~, wherein the sugar moiety of said terminal nucleotide has an oxygen atom at each of the 2' and 3' positions thereof.

207
190
793. The oligo- or polynucleotide of claim ~~775~~, comprising at least one deoxyribonucleotide.

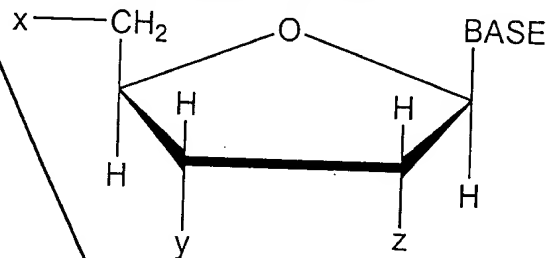
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794. An oligo- or polynucleotide which is complementary to a nucleic acid of interest or a portion thereof, said oligo- or polynucleotide comprising at least one modified nucleotide having the structural formula:



wherein x is selected from the group consisting of H—, HO—, a mono-phosphate, a di-phosphate and a tri-phosphate;

wherein y is selected from the group consisting of H—, HO—, a mono-phosphate, a di-phosphate and a tri-phosphate;

wherein z is selected from the group consisting of H—, HO—, a mono-phosphate, a di-phosphate and a tri-phosphate; and

wherein Sig is covalently attached through a chemical linkage to at least one phosphate selected from the group consisting of x, y and z, and a combination thereof, said chemical linkage comprising a polypeptide or a protein, and said Sig comprising a non-radioactive label moiety which can be directly detected when attached to said phosphate via said polypeptide or protein chemical linkage or when said modified nucleotide is incorporated into said oligo- or polynucleotide, or when said oligo- or polynucleotide is hybridized to said complementary nucleic acid of interest or a portion thereof, provided that when said oligo- or polynucleotide is an

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SUB
025
COU4

oligoribonucleotide or a polyribonucleotide and when Sig is attached through a chemical linkage to a terminal PM at the 3' position of a terminal ribonucleotide, said chemical linkage is not obtained through a 2',3' vicinal oxidation of a 3' terminal ribonucleotide previously attached to said oligoribonucleotide or polyribonucleotide.

N1
COU4

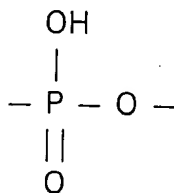
795. The oligo- or polynucleotide of claim 794, wherein said Sig is or renders the nucleotide or the oligo- or polynucleotide self-signaling or self-indicating or self-detecting.

209 208

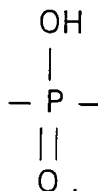
796. The oligo- or polynucleotide of claim 794, wherein said Sig moiety comprises at least three carbon atoms.

210 208

797. The oligo- or polynucleotide of claim 794, wherein said covalent attachment is selected from the group consisting of



and



SUB
030

798. The oligo- or polynucleotide of claim 794, wherein said polypeptide or protein chemical linkage does not interfere substantially with the characteristic ability of Sig to form a detectable signal.

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SUB
O3D
COU¹

799. The oligo- or polynucleotide of claim 794, wherein said x and y each comprise a member selected from the group consisting of a monophosphate, a diphosphate and a triphosphate and Sig moiety is covalently attached to either or both of said x and y a phosphorus atom or a phosphate oxygen.

213

2108

800. The oligo- or polynucleotide of claim 794, wherein Sig comprises a component selected from the group consisting of biotin, iminobiotin, an electron dense component, a magnetic component, a metal-containing component, a fluorescent component, a chemiluminescent component, a chromogenic component or a combination of any of the foregoing.

N¹
COU¹

214

213

801. The oligo- or polynucleotide of claim 800, wherein said electron dense component comprises ferritin.

215

213

802. The oligo- or polynucleotide of claim 800, wherein said magnetic component comprises magnetic oxide.

216

215

803. The oligo- or polynucleotide of claim 802, wherein said magnetic oxide comprises ferric oxide.

217

213

804. The oligo- or polynucleotide of claim 800, wherein said metal-containing component is catalytic.

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²¹⁸
~~805.~~ The oligo- or polynucleotide of claim ~~800~~²¹³, wherein said fluorescent component comprises a member selected from the group consisting of fluorescein, rhodamine and dansyl.

²¹⁶
~~806.~~ The oligo- or polynucleotide of claim 794, wherein said oligo- or polynucleotide is terminally ligated or attached to said polypeptide or protein chemical linkage.

²²⁰
~~807.~~ The oligo- or polynucleotide of claim ~~794~~²⁰⁸, wherein said polypeptide comprises polylysine.

²²¹
~~808.~~ The oligo- or polynucleotide of claim ~~794~~²⁰⁸, wherein said polypeptide is selected from the group consisting of avidin, streptavidin and anti-hapten immunoglobulin.

²²³
~~809.~~ The oligo- or polynucleotide of claim 794, wherein said Sig moiety is attached via said polypeptide or protein chemical linkage to a terminal nucleotide in said oligo- or polynucleotide.

²²³
~~810.~~ The oligo- or polynucleotide of claim ~~809~~²²², wherein z of said terminal nucleotide comprises a hydrogen atom at the 2' position thereof.

²²⁴
~~811.~~ The oligo- or polynucleotide of claim ~~809~~²²², wherein both y and z of said terminal nucleotide comprise an oxygen atom at each of the 3' and 2' positions thereof, respectively.

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225

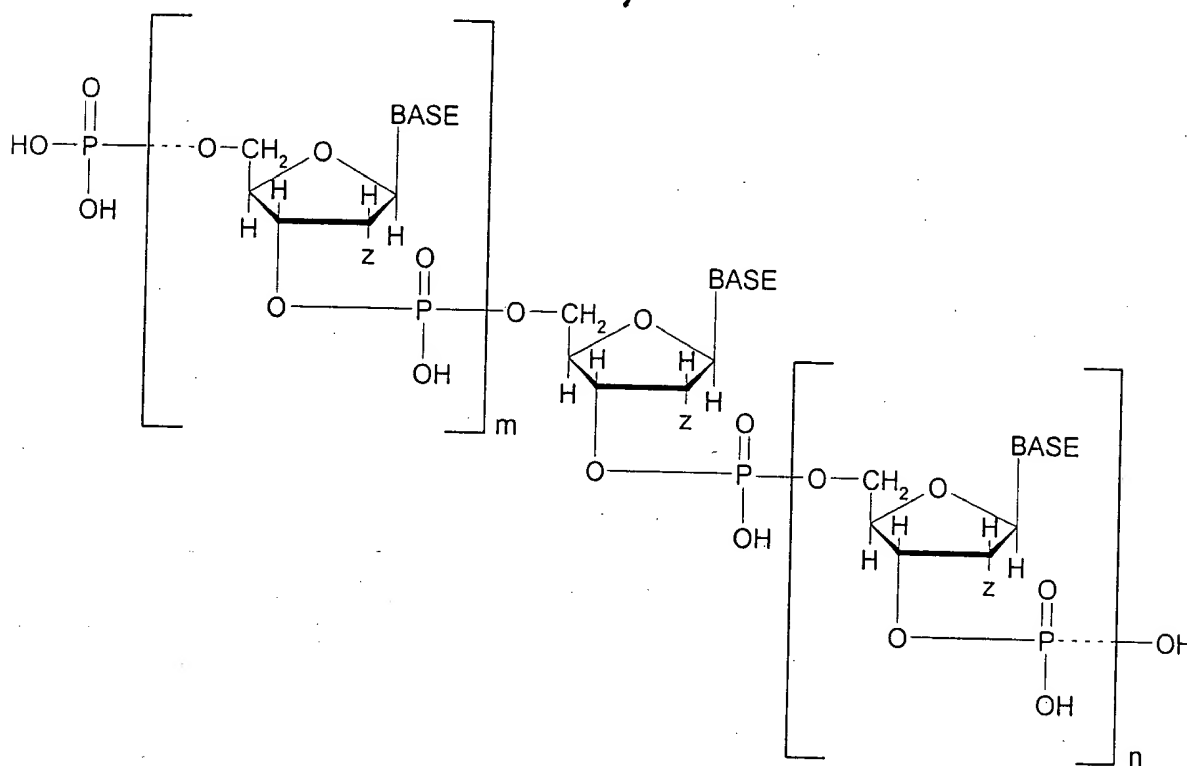
~~812.~~ The oligo- or polynucleotide of claim ~~794~~, comprising at least one deoxyribonucleotide.

208

226

~~813.~~ The oligo- or polynucleotide of claim ~~794~~, having the structural formula:

208



wherein m and n represent integers from 0 up to about 100,000, and wherein said Sig moiety is attached to at least one of the phosphate moieties in said structural formula.

~~814.~~ The oligo- or polydeoxyribonucleotide of claims 454 or 658, wherein said Sig is covalently attached to PM through a chemical linkage comprising a polypeptide or a protein.

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228

227

~~815.~~ The oligo- or polydeoxyribonucleotide of claim ~~814~~, wherein said polypeptide comprises polylysine.

SUB
034

~~816.~~ The oligo- or polydeoxyribonucleotide of claim 814, wherein said polypeptide or protein is selected from the group consisting of avidin, streptavidin and anti-hapten immunoglobulin.

230

20 97

~~817.~~ The oligo- or polydeoxyribonucleotide of claims ~~586~~ or ~~677~~, wherein said Sig is covalently attached to said at least one phosphate through a chemical linkage comprising a polypeptide or a protein.

N'
CONT.

231

230

~~818.~~ The oligo- or polydeoxyribonucleotide of claim ~~817~~, wherein said polypeptide comprises polylysine.

~~819.~~ The oligo- or polydeoxyribonucleotide of claim 817, wherein said polypeptide or protein is selected from the group consisting of avidin, streptavidin and anti-hapten immunoglobulin.

SUB
035

~~820.~~ The oligo- or polynucleotide of claims 617 or 697, wherein said Sig is covalently attached to PM via a chemical linkage comprising a polypeptide or a protein.

234

233

~~821.~~ The oligo- or polydeoxyribonucleotide of claim ~~820~~, wherein said polypeptide comprises polylysine.

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SUB
036
822. The oligo- or polydeoxyribonucleotide of claim 820, wherein said polypeptide or protein is selected from the group consisting of avidin, streptavidin and anti-hapten immunoglobulin.

N'
CDV4
823. The oligo- or polynucleotide of claims 637 or 716, wherein said Sig is covalently attached to said at least one phosphate through a chemical linkage comprising a polypeptide or a protein.

237
236
824. The oligo- or polydeoxyribonucleotide of claim 823, wherein said polypeptide comprises polylysine.

SUB
037
825. The oligo- or polydeoxyribonucleotide of claim 824, wherein said polypeptide or protein is selected from the group consisting of avidin, streptavidin and anti-hapten immunoglobulin.

✓
Cancel claims 454-567.

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